UNITED STATES PATENT & TRADEMARK OFFICE

Appl. No.	:	10/045,607
Applicant	:	Lino TAVARES et al.
Filed	:	October 23, 2001
A.U.	:	1615
Examiner	:	GHALI, Isis A D
For:	:	**LORATADINE TRANSDERMAL DEVICE AND METHODS**
Docket No.	:	208.1004US
Customer No.	:	23280

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

January 25, 2006

APPELLANTS BRIEF ON APPEAL UNDER 37 C.F.R. §1.192

Sir:

Appellants submit this brief for the consideration of the Board of Patent Appeals and Interferences in support of their appeal of the Final Rejection dated July 28, 2005 in the above-identified application. A Notice of Appeal and a Petition for a Three Month Extension of Time are filed herewith. An original and two copies of this brief are submitted herewith. A fee in the amount of $2,020.00 is paid concurrently herewith, $500.00 of which covers the statutory fee for the Notice of Appeal, $500.00 of which covers the statutory fee for filing this brief in support of the appeal, and $1,020.00 of which covers the statutory fee for the Petition for the three month extension of time.

I. REAL PARTY IN INTEREST

The real party in interest is Purdue Pharma LP, having a place of business at One Stamford Forum, Stamford, Connecticut 06901-3431, assignee of the entire right, title and interest in the above-identified patent application.

II. RELATED APPEALS AND INTERFERENCES

Appellants and their legal representatives and assignee are not aware of any appeal or interference that directly affects, will be directly affected by, or will have a bearing on the decision in this appeal.

III. STATUS OF CLAIMS

Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-38, and 40-49 are currently pending and are subject to a final rejection, dated July 28, 2005. Claims 1-7, 12, 15, 17-19, 21, 25-28, 31 and 39 were previously cancelled. This appeal is taken from this final rejection. Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-38, and 40-49 remain in the application and are appealed. A copy of these appealed claims is attached hereto as an Appendix.

IV. STATUS OF AMENDMENTS

In the Amendment under 37 C.F.R. § 1.111, dated May 9, 2005, claims 46-49 were added. Claims 1-7, 12, 15, 17-19, 21, 25-28, 31 and 39 were previously cancelled. The claims have not been amended after the Final Rejection of July 28, 2005.

V. SUMMARY OF INVENTION

The present invention is directed to transdermal delivery systems containing loratadine or a pharmaceutically acceptable salt thereof, or methods of using a transdermal delivery system, which provide (i) *specific* mean relative release rates as determined via an in-vitro permeation test and (ii) *specific* plasma levels when administered to a human patient.

In the following arguments, Appellants contrast this invention to the two remaining prior art references cited by the Examiner, which, to the extent that they teach a transdermal delivery system of loratadine for the treatment of allergic conditions, fail to teach or suggest the specific pharmacokinetic parameters and release rates provided by the transdermal device of the present invention.

VI. ISSUES

The following issues are presented for appeal:

(1) Whether claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 are unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 4,910,205 to Kogan et al.

(2) Whether claims 37, 38, 44, and 45 are unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent 5,240,711 to Hille et al.

VII. GROUPING OF CLAIMS

The Examiner has rejected claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 as a single group. However, Appellants believe that claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 may be divided into three (3) groups for appeal. As argued below, Appellants assert that these groups of claims are separately patentable, and the claims of each group stand or fall together.

Group I includes claims 8-11, 13, 14, 16 and 47 as a single group

Group II includes claims 20-24, 29, 30, 32-38, 40-45 and 48 as a single group.

Group III includes claims 46 and 49 as a single group.

Appellants believe that these groupings of claims are separately patentable, as the claims of Group I are directed to methods for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with transdermal delivery systems containing loratadine; the claims of Group II are directed to transdermal delivery systems containing loratadine which provide certain release rates and certain plasma levels of loratadine; and the claims of Group III are directed to a method of treating seasonal allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering to a human patient loratadine transdermally wherein the transdermal delivery device includes a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof.

Appellants submit that the methods and devices of Groups I and II, respectively, can include materially different ingredients in the reservoir layer than the devices of the methods of Group III. For example, the methods of Group III recite a administering a transdermal delivery device containing loratadine or pharmaceutically acceptable salt thereof and including a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof, whereas the methods of the claims of Group I and the devices of the claims of Group II are not limited to only these ingredients in the reservoir.

Appellants believe that these three groups of claims are separately patentable.

VIII. ARGUMENT

A. 35 U.S.C. § 103(a) Rejection of Claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, 40-49 Based on U.S. Patent No. 4,910,205 to Kogan et al.

1. The Examiner's rejection

The first issue presented is whether claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38 and 40-49 are unpatentable under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 4,910,205 to Kogan et al. ("Kogan").

In the Final Office Action, the Examiner asserted the following:

> [I]t would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal device to deliver loratadine to treat allergic conditions as disclosed by US '205, *and adjust the dose* to deliver a specific desired plasma profile according to the patient's need, motivated by the teachings of US '205 that the dose may be varied depending on the size and age of the patient, and may also depends upon the severity of the condition being treated, with reasonable expectation of having a transdermal drug delivery device that delivers loratadine at the desired levels and treats allergic conditions effectively.

Final Office Action at page 4 (emphasis added).

2. U.S. Patent No. 4,910,205 does not render the claims obvious

Appellants respectfully submit that Kogan fails in the very least to teach or suggest the following claimed relative release rates recited in the present claims as determined by the Valia-Chien cell:

> said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;
>
> from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;
>
> from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours;

and a mean relative release rate of from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours

While the Valia-Chien cell might have been known to one skilled at the art at the time of the invention, the prior art is absolutely silent about the claimed relative release rates as determined by the Valia-Chien cell. Moreover, the prior art of record does not even apply the Valia-Chien cell to transdermal delivery systems containing loratadine. Thus, the prior art cited by the Examiner cannot teach or suggest specific mean relative release rates claimed in the present invention.

In the Final Office Action, the Examiner acknowledged that the Kogan "does not teach the specific delivery profile of loratadine, the specific amounts of different ingredients, or specific solvents and softening agents in the transdermal delivery system." Final Office Action at page 3 (*emphasis added*). The examiner also acknowledges that the prior art would need to be adjusted in order to deliver the claimed plasma profile. See Final Office Action at page 4. Accordingly, Appellants respectfully disagree with the Examiner's later position that "it is expected to have the same delivery profile from a transdermal delivery device disclosed by the prior art that has the same composition and the same amount or loratadine." Id.

Appellants further submit that the Examiner relied on impermissible hindsight vision in reconstructing the present invention. The Examiner stated that it is "within the skill in the art to select optimal parameters in order to achieve a beneficial effect," Final Office Action at page 3. The Examiner also asserted that "motivation to modify the dose would have been driven from the teaching of US '205 that the dose may be varied depending on the size and age of the patient, and may also depends upon the severity of the conditions being treated, with reasonable expectation of having a transdermal drug delivery device that delivers loratadine at the desired levels and treats allergic conditions effectively." Final Office Action at page 6. However, the Examiner has failed to provide motivation to one skilled in the art to formulate a transdermal delivery system which provides the specific relative in-vitro release rates and the specific blood plasma level recited in the present claims, and has also failed to provide motivation to one skilled in

the art to utilize the methods for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with such transdermal delivery systems. It is respectfully submitted that only in view of the teachings of the present application would one of ordinary skill in the art be motivated to formulate the transdermal delivery systems or utilize the methods of treatment as recited in the present claims.

As the Examiner has failed to provide motivation to manipulate the prior art in order to arrive at either the claimed transdermal delivery systems containing loratadine or the claimed methods for treating allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient with such transdermal delivery systems, Appellants respectfully request that the obviousness rejection over Kogan be withdrawn.

Appellants note that the release rates as determined by the Valia-Chien cell recited in the claims are limitations of the transdermal delivery systems and methods of the present claims. Further, Appellants respectfully submit that "[a] functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used." MPEP 2173.05(g), Eighth Edition, Revision 2.

With respect to Group III, Appellants respectfully submit that claim 46, which recites in part, "a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof" (*emphasis added*), is separately patentable over Kogan et al. Appellants respectfully submit that Kogan is directed to the surprising result provided by a loratadine transdermal device which contains a combination of a volatile solvent, an essential oil and a fatty acid ester. See Kogan et al., col. 1, lines 54-59. Therefore, after reading Kogan, one skilled in the art would not be motivated to utilize a device that does not contain an essential oil, such as the system as recited in independent claim 46. Thus, claim 46, and Group III is patentable over Kogan.

For the foregoing reasons, Appellants believe that independent claims 8, 20 and 46 are patentable over Kogan and respectfully request that 35 U.S.C. § 103 (a) rejection over these claims be reversed. As claims 9-11, 13, 14, 16, 21-24, 29, 30, 32-38, 40-45, and 47-49 depend from either independent claim 8, 20 or 46, and include all the limitations of the independent claim they depend on, Appellants submit that the rejections of these dependent claims should be reversed.

B. 35 U.S.C. §103 (a) Rejection of claims 37, 38, 44 and 45 Based on U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al.

Claims 37, 38, 44 and 45 were rejected under 35 U.S.C. § 103 (a) on the grounds of being unpatentable over Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al. Claims 37, 38, 44 and 45 all depend from claim 23, which is dependent on claim 20.

1. The Examiner's rejection

The second issue presented is whether claims 37, 38, 44 and 45 are unpatentable under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent 5,240,711 to Hille et al. ("Hille").

In the Final Office Action, the Examiner stated the following:

> [I]t would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic conditions using a transdermal device comprising loratadine that provides a specific delivery profile and having particular structure as disclosed by US '205, *and select* the specific solvents and softening agents disclosed by US '711, motivated by the teaching of US '711 that the transdermal device having these particular ingredients in its reservoir layer provides a controlled delivery of the drug, with reasonable expectation of having a transdermal drug delivery device to deliver loratadine to treat allergic conditions effectively.

Final Office Action at pages 7-8 (emphasis added).

2. U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al. does not render the claims obvious

Appellants respectfully submit that Hille describes the use of burpenorphine as the active agent, and fails to teach or suggest the use of any other active agent, such as loratadine. Therefore, Appellants submit that Kogan and Hille are improperly combinable, as one of skill in the art would not look to combine a reference directed to the treatment of seasonal allergies with a reference directed to the treatment of pain.

Appellants additionally submit that even if the references were properly combinable, the Examiner is improperly picking and choosing a specific element of Kogan, i.e. loratadine, and combining it with the transdermal delivery device of Hille. One "...cannot pick and chose among the individual elements of assorted prior art references to recreate the claimed invention." Smith Kline Diagnostics, Inc. v. Helena Laboratories Corporation, 859 F. 2d 878, 887 (Fed. Cir. 1988).

Furthermore, Hille fails to cure the deficiencies of Kogan (e.g., claimed specific relative release rates; specific blood plasma levels recited in the claims, etc.), as discussed above. Therefore, Appellants respectfully request that §103(a) Rejection based on U.S. Patent No. 4,910,205 to Kogan et al. in view of U.S. Patent No. 5,240,711 to Hille et al. of claims 37, 38, 44 and 45 be removed.

C. Conclusion

Appellants' claimed loratadine containing transdermal delivery systems and the use of said systems in methods of treating allergic conditions are substantially different from the formulations and methods described in Kogan et al. and Hille et al., individually or combined. The claimed transdermal delivery systems and methods have limitations which are neither taught nor suggested by either Kogan et al. and/or Hille et al. Appellants believe that, for the foregoing reasons, the final rejections of claims should be reversed.

Prompt consideration of the arguments presented herein and reversal of the final rejections is earnestly solicited.

Respectfully submitted,
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IX. APPENDIX

LISTING OF CLAIMS

Claims 1-7. (Cancelled)

Claim 8. (Previously Presented) A method of effectively treating seasonal allergic rhinitus, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering loratadine transdermally to the human patient by applying a transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval, said transdermal delivery device maintaining a plasma level of loratadine at steady state from about 1 to about 3 ng/ml;

said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours;

and a mean relative release rate of from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 9. (Original) The method of claim 8 wherein the plasma level of loratadine at 48 hours does not decrease by more than 30% over the next 72 hours.

Claim 10. (Original) The method of claim 8, further comprising maintaining an effective mean relative release rate of said transdermal delivery system to provide a substantially first order plasma level increase of loratadine from the initiation of the dosing interval

until about 48 to about 72 hours after the initiation of the dosing interval; and thereafter providing an effective mean relative release rate to provide a substantially zero order plasma level fluctuation of loratadine until the end of at least the five-day dosing interval.

Claim 11. (Original) The method of claim 8, further comprising providing a mean relative release rate of loratadine from said transdermal delivery system to provide a plasma level of loratadine of at least about 0.1 ng/ml within about 6 hours after application of said transdermal delivery system onto the skin of the patient.

Claim 12. (Cancelled)

Claim 13. (Original) The method of claim 8, wherein said therapeutic plasma level is maintained from about 0.1 ng/ml to about 3.3 ng/ml during the dosing interval for said transdermal delivery system.

Claim 14. (Original) The method of claim 8, wherein said transdermal delivery system has a mean relative release rate from about 1.0 $\mu g/hour/cm^2$ to about 30.0 $\mu g/hour/cm^2$.

Claim 15. (Cancelled)

Claim 16. (Original) The method of claim 8, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 63 $\mu g/cm^2$ to about 388 $\mu g/cm^2$ at 24 hours; from about 105 $\mu g/cm^2$ to about 660 $\mu g/cm^2$ at 48 hours; and from about 139 $\mu g/cm^2$ to about 854 $\mu g/cm^2$ at 72 hours; and from about 162 $\mu g/cm^2$ to about 955 $\mu g/cm^2$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

Claims 17-19 (Cancelled)

Claim 20. (Previously Presented) A transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof which provides a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 $\mu g/cm^2/hr$ to about 11.9 $\mu g/cm^2/hr$ at 72 hours; and

from about 1.8 $\mu g/cm^2/hr$ to about 9.9 $\mu g/cm^2/hr$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell having a receptor chamber containing a 40:60 mixture of ethanol:water; said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within 36 hours from the initiation of the dosing interval, and a plasma level of loratadine of at least about 0.1 ng/ml by about 6 hours after application of said transdermal delivery system onto the skin of a human patient; said transdermal delivery system maintaining a therapeutic blood level until the end of at least a five-day dosing interval and a plasma level of loratadine at steady-state from about 1 to about 3 ng/ml.

Claim 21. (Cancelled)

Claim 22. (Original) The transdermal delivery system of claim 20, which provides an in-vitro cumulative amount of permeation of from about 63 $\mu g/cm^2$ to about 388 $\mu g/cm^2$ at 24 hours; from about 105 $\mu g/cm^2$ to about 660 $\mu g/cm^2$ at 48 hours; and from about 139 $\mu g/cm^2$ to about 854 $\mu g/cm^2$ at 72 hours, as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 23. (Original) The transdermal delivery system of claim 20, comprising a backing layer which is impermeable to the active substance, a pressure-sensitive adhesive reservoir layer, and optionally a removable protective layer, the reservoir layer by weight comprising 20 to 90% of a polymeric matrix, 0.1 to 30% of a softening agent, 0.1 to 20% of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% of a solvent for the loratadine or salt thereof.

Claim 24. (Original) The transdermal delivery system of claim 20, which is a laminated composite comprising (a) a polymer backing layer that is substantially impermeable to loratadine or the pharmaceutically acceptable salt thereof; and (b) a reservoir layer comprising an acrylate or silicone based pressure-sensitive adhesive, 0.1 to 20% of loratadine base or of a pharmaceutically acceptable salt thereof, 0.1 to 30% of an ester of a carboxylic acid acting as a softening agent and 0.1 to 30% of a solvent for loratadine having at least one acidic group.

Claims 25-28. (Cancelled)

Claim 29. (Previously Presented) The transdermal delivery system of claim 20, wherein said therapeutic plasma level is maintained from about 0.1 ng/ml to about 3.3 ng/ml during the dosing interval for said transdermal delivery system.

Claim 30. (Previously Presented) The transdermal delivery system of claim 20, wherein said transdermal delivery system has a mean relative release rate from about 1.0 $\mu g/hour/cm^2$ to about 30.0 $\mu g/hour/cm^2$.

Claim 31. (Cancelled)

Claim 32. (Previously Presented) The transdermal delivery system of claim 20, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 63 $\mu g/cm^2$ to about 388 $\mu g/cm^2$ at 24 hours; from about 105 $\mu g/cm^2$ to about 660 $\mu g/cm^2$ at 48 hours; and from about 139 $\mu g/cm^2$ to about 854 $\mu g/cm^2$ at 72 hours; and from about 162 $\mu g/cm^2$ to about 955 $\mu g/cm^2$ at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 33. (Original) The transdermal delivery system according to claim 23, wherein the backing layer is composed of a flexible material.

Claim 34. (Original) The transdermal delivery system according to claim 23, wherein the backing layer is selected from the group consisting of a flexible material, an inflexible material, and an aluminum foil.

Claim 35. (Previously Presented) The transdermal delivery system according to claim 23, wherein the polymeric matrix is at least one of rubber, a synthetic homo-, co- or blockpolymer, a urethane and silicone.

Claim 36. (Original) The transdermal delivery system according to claim 23, wherein the softening agent is at least one of dodecanol, undecanol, octanol, a glycol and glycanol.

Claim 37. (Original) The transdermal delivery system according to claim 23, wherein the solvent is a monoester of a dicarboxylic acid.

Claim 38. (Original) The transdermal delivery system according to claim 23, wherein the solvent is at least one of monomethyl glutarate and monomethyl adipate.

Claim 39. (Cancelled)

Claim 40. (Original) The transdermal delivery system according to claim 23, wherein by weight the polymer is present in about 55%, the loratadine in about 10%, the solvent in about 10% and the softener in about 15%.

Claim 41. (Original) A transdermal delivery system according to claim 23, wherein the solvent is present in from about 25 to 100% the weight of the loratadine.

Claim 42. (Original) The transdermal delivery system according to claim 23, which also comprises a removable protective layer.

Claim 43. (Original) The transdermal delivery system according to claim 23, wherein the pressure-sensitive adhesive reservoir layer comprises a polymer based on an acrylate, a methacrylate, a silicone compound or a combination thereof.

Claim 44. (Previously Presented) The transdermal delivery system according to claim 23, wherein the softening agent is a medium-chain triglyceride of the caprylic/capric acids of coconut oil.

Claim 45. (Original) The transdermal delivery system according to claim 23, wherein the solvent has at least one acidic group.

Claim 46. (Previously presented) A method of effectively treating seasonal allergic rhinitus, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering loratadine transdermally to the human patient by applying a transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval, said transdermal delivery device maintaining a plasma level of loratadine at steady state from about 1 to about 3 ng/ml;

said transdermal delivery device comprising a backing layer which is substantially impermeable to the loratadine or pharmaceutically acceptable salt thereof; and a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent, 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent for the loratadine or salt thereof;

said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu g/cm^2/hr$ to about 16.2 $\mu g/cm^2/hr$ at 24 hours;

from about 2.3 $\mu g/cm^2/hr$ to about 13.7 $\mu g/cm^2/hr$ at 48 hours;

from about 2.0 μg/cm^2/hr to about 11.9 μg/cm^2/hr at 72 hours;

and a mean relative release rate of from about 1.8 μg/cm^2/hr to about 9.9 μg/cm^2/hr at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin , said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 47. (Previously Presented) The method of claim 8, wherein said transdermal delivery system has a mean relative release rate of from about 1.5 μg/cm^2/hr to about 8.5 μg/cm^2/hr at 120 hours;

from about 2.4 μg/cm^2/hr to about 7.7 μg/cm^2/hr at 144 hours;

and from about 1.5 μg/cm^2/hr to about 6.7 μg/cm^2/hr at 168 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 48. (Previously Presented) The transdermal delivery system of claim 20, wherein said transdermal delivery system has a mean relative release rate of from about 1.5 μg/cm^2/hr to about 8.5 μg/cm^2/hr at 120 hours;

from about 2.4 μg/cm^2/hr to about 7.7 μg/cm^2/hr at 144 hours;

and from about 1.5 μg/cm^2/hr to about 6.7 μg/cm^2/hr at 168 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Claim 49. (Previously Presented) The method of claim 46, wherein said transdermal delivery system has a mean relative release rate of from about 1.5 μg/cm^2/hr to about 8.5 μg/cm^2/hr at 120 hours;

from about 2.4 μg/cm^2/hr to about 7.7 μg/cm^2/hr at 144 hours;

and from about 1.5 μg/cm^2/hr to about 6.7 μg/cm^2/hr at 168 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a

human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.